Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Aug-2023
Document Type: USP Monographs
DocId: GUID-A24085EB-7D18-41BB-9FBE-7BCE1E48A502_5_en-US
DOI: https://doi.org/10.31003/USPNF_M65015_05_01
DOI Ref: 8ic8r

Pilocarpine Hydrochloride Tablets

DEFINITION

Pilocarpine Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of pilocarpine hydrochloride ($C_{11}H_{16}N_2O_2 \cdot HCl$).

IDENTIFICATION

• **A.** The retention time of the major peak of the *Sample solution* corresponds to the major peak of the *Standard solution*, as obtained in the *Assay*.

• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: 10 N sodium hydroxide, 85% phosphoric acid, triethylamine, and water (7:6:1:500). Adjust with 10 N sodium hydroxide to a pH of 3.0.

Mobile phase: Methanol and *Solution A* (3:100)

Standard solution: 50 µg/mL of USP Pilocarpine Hydrochloride RS

System suitability solution: Transfer 10 mL of the *Standard solution* to a test tube. Add 100 µL of 2 N sodium hydroxide, mix well, and allow it to stand for 5 min. Add 100 µL of 2 N hydrochloric acid and mix well. [Note—This preparation contains pilocarpine, isopilocarpine, and two unidentified compounds.]

Sample stock solution: Nominally 0.1 mg/mL of pilocarpine hydrochloride in water prepared as follows. Place Tablets, equivalent to 50 mg of pilocarpine hydrochloride, in a 500-mL volumetric flask. Fill the flask 75% full with water. Stir for at least 30 min or more if necessary, until the Tablets are completely disintegrated and the powder is finely dispersed. Dilute with water to volume.

Sample solution: Nominally 50 µg/mL of pilocarpine hydrochloride in water from *Sample stock solution*. Pass a suitable amount of solution through a PVDF filter of 0.45-µm pore size, and discard the first 5 mL of the filtrate.

Chromatographic system

(See *Chromatography (621), System Suitability*.)

Mode: LC

Detector: UV 215 nm. For *Identification B*, use a diode array detector in the range of 190–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Samples: *Standard solution* and *System suitability solution*

[Note—The relative retention times for isopilocarpine, pilocarpine, and two unidentified peaks are 0.9, 1.0, 1.2, and 1.5, respectively.]

Suitability requirements

Resolution: NLT 1.2 between isopilocarpine and pilocarpine; NLT 1.2 between pilocarpine and the peak at a relative retention time of 1.2; NLT 1.2 between the peaks at relative retention times of 1.2 and 1.5, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pilocarpine hydrochloride ($C_{11}H_{16}N_2O_2 \cdot HCl$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of pilocarpine hydrochloride from the *Sample solution*

r_S = peak response of pilocarpine hydrochloride from the *Standard solution*

C_S = concentration of USP Pilocarpine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of pilocarpine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm

Time: 45 min

Buffer solution: 13.5 mL of *phosphoric acid* and 3.0 mL of triethylamine in 1000 mL of *water*. Adjust with phosphoric acid or 10 N sodium hydroxide to a pH of 3.

Mobile phase: *Methanol* and *Buffer solution* (3:17)

Standard stock solution: 0.1 mg/mL of USP Pilocarpine Hydrochloride RS in *Medium*

Standard solution

For Tablets labeled to contain 7.5 mg: Transfer 15.0 mL of the *Standard stock solution* to a 100-mL volumetric flask, and dilute with *Medium* to volume.

For Tablets labeled to contain 5 mg: Transfer 5.0 mL of the *Standard stock solution* to a 50-mL volumetric flask, and dilute with *Medium* to volume.

Sample solution: Pass the solution under test through a suitable polyethylene filter of 45-µm pore size.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of pilocarpine hydrochloride ($C_{11}H_{16}N_2O_2 \cdot HCl$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 mL

Tolerances: NLT 75% (Q) of the labeled amount of pilocarpine hydrochloride ($C_{11}H_{16}N_2O_2 \cdot HCl$) is dissolved.

Change to read:

• **Uniformity of Dosage Units ⟨905⟩:** ▲Meet the requirements▲ (CN 1-Aug-2023)

Procedure for content uniformity

Mobile phase, Standard solution, System suitability solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Sample solution: Place 1 Tablet in a suitable volumetric flask, fill the flask about 75% full with *water*, and vigorously stir for NLT 30 min to ensure complete disintegration. Dilute with water to volume to obtain a final concentration of 0.05 mg/mL of pilocarpine hydrochloride. Pass the solution through a PVDF filter of 0.45-µm pore size.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pilocarpine hydrochloride ($C_{11}H_{16}N_2O_2 \cdot HCl$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of pilocarpine hydrochloride from the *Sample solution*

r_S = peak response of pilocarpine hydrochloride from the *Standard solution*

C_S = concentration of USP Pilocarpine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of pilocarpine hydrochloride in the *Sample solution* (mg/mL)

▲▲ (CN 1-Aug-2023)

IMPURITIES

• **Organic Impurities**

Procedure

Mobile phase, System suitability solution, Sample stock solution, and **System suitability:** Proceed as directed in the *Assay.*

Standard solution: 0.5 µg/mL of USP Pilocarpine Hydrochloride RS

Sample solution: Nominally 100 µg/mL of pilocarpine hydrochloride in water from *Sample stock solution*. Pass a suitable amount of solution through a PVDF filter of 0.45-µm pore size, and discard the first 5 mL of the filtrate.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 100 µL

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of pilocarpine hydrochloride from the *Standard solution*

C_S = concentration of USP Pilocarpine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of pilocarpine hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor for each impurity (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Isopilocarpine	0.9	0.79	1.0

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Pilocarpine	1.0	1.0	—
Pilocarpic acid	1.2	1.0	0.5
Any individual unspecified impurity	—	1.0	0.2
Total impurities	—	—	1.2

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩
  USP Pilocarpine Hydrochloride RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
PILOCARPINE HYDROCHLORIDE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(3)

Current DocID: GUID-A24085EB-7D18-41BB-9FBE-7BCE1E48A502_5_en-US

DOI: https://doi.org/10.31003/USPNF_M65015_05_01

DOI ref: 8ic8r